Remarks

The January 8, 2008, Official Action and the references cited therein have been carefully reviewed. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set forth in the January 8, 2008, Official Action. Therefore, the initial due date for response is April 8, 2008. A petition for a one (1) month extension of the response period is presented with this response, which is being filed within the one month extension period.

Applicants note that the Examiner has deemed the restriction requirement proper and made it final. Therefore, claims 1-8, 11, 13-18, 26, 28-35, 38, 42-45 are withdrawn from consideration, and claims 9-10, 12, 19-25, 27, 36-37, and 46-52 have been examined on the merits.

As a preliminary matter, at page 4 of the Official Action, the Examiner has objected to the specification and indicates that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 because Figure 5 contains sequence information without any sequence identifiers. In response, Applicants have amended the brief description of the drawings in the specification to include the appropriate sequence identifiers. Applicants submitted a paper copy and electronic copy of the sequence listing in full compliance with 37 C.F.R. §§1.821-1.825 which lists the sequences shown in Figure 5 on May 23, 2007. Accordingly, the attached Notice to comply is in error as only the specification requires amendment at this time. If Applicants' understanding is in error, the Examiner is requested to contact the undersigned who will immediately refile the previously filed paper which included the paper copy, the

electronic copy of the sequences and the requisite verification statement.

Turning to the substantive aspects of the January 8, 2008, Official Action, at page 5, the Examiner has rejected claims 9, 12, 19-25, 27, 36-37 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claim 9 stands rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Magliaccio et al. (EMBO Journal, (1997) 16:706-716).

Lastly, the Examiner has rejected claims 9-10, 12, 19-25, 27, 36-37, and 46-52 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The foregoing objections and rejections constitute all of the grounds set forth in the January 8, 2008, Official Action for refusing the present application. Applicants respectfully request reconsideration of this application and the timely allowance of pending claims 9-10, 22-25, 27, 36-37, 46-47, and 52 in view of the claim amendments and arguments set forth below.

THE CLAIMS, AS AMENDED, SATISFY THE REQUIREMENTS OF 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 9, 12, 19-25, 27, and 36-37, asserting that they are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The relevant inquiry in determining whether a given claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is whether the claim sets out and circumscribes a particular area with a reasonable degree of precision and particularity such that the metes and bounds of the claimed

invention are reasonably clear. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971). Applicants respectfully submit that with respect to the amended claims of the present application, such inquiry must be answered in the affirmative.

At page 5 of the Official Action, the Examiner states that method claims require an active or positive step that accomplishes the goals for the method which are stated in the preamble. Inasmuch as the original claims allegedly lacked an active or positive step, the Examiner has deemed the claims indefinite. In response, Applicants have amended independent claims 9, 22, and 36 to recite an active or positive step at the end of the claim which relates the last step to the preamble of the claim. The claims have been further amended to remove any perceived ambiguity. Claims 23 and 25 have been cancelled thereby rendering the rejection of these claims moot.

In light of the foregoing remarks and claim amendment, Applicants respectfully submit that the metes and bounds of the claims are clear to the skilled person. Accordingly, it is requested that the above-mentioned rejection under 35 U.S.C. §112, second paragraph be withdrawn.

CLAIM 9, AS AMENDED, IS NOT ANTICIPATED BY MIGLIACCIO ET AL.

The Examiner has rejected claim 9 under 35 U.S.C. §102(b) as allegedly being anticipated by Migliaccio et al. (EMBO Journal, (1997) 16:706-716). It is the Examiner's position that Migliaccio et al. teach transfecting a cell line with a plasmid which expresses $p66^{SHC}$.

Applicants respectfully disagree with the Examiner's position and submit that Migliaccio et al. fail to disclose a method identical to that of amended claim 9. It is a well-settled premise in patent law that in order to constitute evidence of lack of novelty under 35 U.S.C. §102(b), a prior

art reference must identically disclose each and every element of the rejected claim. In re Bond, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990).

Applicants have amended claim 9 to recite that the agent introduced into the cell is a nucleic acid molecule capable of hybridizing to a nucleic acid encoding SEQ ID NO: 2, thereby modulating resistance to oxidative stress. Support for this amendment can be found throughout the specification, for example, at page 13, lines 4-12. Applicants submit that this amendment renders the §102 rejection over Migliaccio et al. moot as this reference does not disclose such a capability of the plasmid expressing $p66^{SHC}$ used in the reference. For this reason, at least, Applicants submit that the Examiner's rejection based on Migliaccio et al. is improper.

As summarized in M.P.E.P. §2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Applicants respectfully submit that the Examiner's reliance on Migliaccio et al. as evidence of anticipation in this case is misplaced when viewed in light of MPEP at §2112 states that: "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (P.T.O. B.P.A.I. 1990)(emphasis in original).

Inherent anticipation requires inevitability. Therefore, to be inherent the result must be inevitable from the disclosure or the inherent characteristic must undeniably be

present in the invention. *Pingree v. Hull*, 518 F.2d 624, 627 (C.C.P.A. 1975) (declaring "where support must be based on an inherent disclosure, it is not sufficient that a person following the disclosure might obtain the result … it must inevitably happen"). Moreover, the Examiner provides no evidence for the assertion that the "method of Migliaccio would necessarily modulate resistance to oxidative stress in a cell". It not at all clear that overexpression of plasmids encoding $p66^{shc}$ or fragments thereof would alter resistance to oxidative stress as presently claimed. That being the case, Migliaccio et al. cannot properly be held to support the present rejection. *Transclean Corp. v. Bridgewood Services, Inc*, 290 F.3d 1364, 1373 (Fed. Cir. 2002) ("anticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation…"). The Examiner improperly interprets Migliaccio et al. as effectively precluding the patentability of any method claim using nucleic acids which hybridize to SEQ ID NO: 2 as a therapeutic agent for modulating oxidative stress resistance in cells.

As stated in MPEP §2112, "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993)." "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 49 U.S.P.Q.2d 1949, 1950-51, (Fed. Cir. 1999).

While Migliaccio et al. disclose the use of plasmids encoding p66shc and fragments thereof in efforts to elucidate the effects of the different isoforms on EGF receptor-MAP kinase-fos signaling, these investigators were concerned the structural organization of p66 and had no appreciation

whatsoever that disruption of p66 signaling would modulate resistance to oxidative stress. Applicant claims are drawn to methods of modulating resistance to oxidative stress, whereas Migliaccio et al. do not mention "oxidative stress," and generally are silent regarding the desirability and feasibility of such modulation.

Furthermore, the Examiner may not rely on the concept of inherency to rewrite the disclosure of a prior art reference. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). It is the Applicants' specification, as opposed to Migliaccio et al., that teaches use of nucleic acid agents which hybridize to SEQ ID NO: 2 for modulating resistance to oxidative stress.

There is also considerable precedent that supports Applicants' position that Migliaccio et al. does not constitute an anticipation of claim 9. For example, in *In re Marshall*, 198 U.S.P.Q. 344 (C.C.P.A. 1978), the Court of Customs and Patent Appeals reversed a §102 rejection of claims directed to a weight control process using a compound which was previously taught by the Physicians Desk reference (PDR) to be effective for the treatment of esophagitis, gastritis, peptic ulcer, and irritable colon syndrome. The rationale for the Court's decision was simply stated as follows: "Nothing in the PDR remotely suggests taking oxethazine to lose weight. If anyone ever lost weight by following the PDR teachings it was an unrecognized accident. An accidental or unwitting duplication of an invention cannot constitute an anticipation." See also *Merck & Co. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367, 1372 (Fed. Cir. 2003) (no anticipation where prior art reference stated generally that a composition might be useful for pharmaceutical preparations yet failed to disclose use of the composition for the claimed method of bone therapy); *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005)(no anticipation where claims

directed to applying a composition to treat sunburn because prior art disclosed applying the composition to skin, but did not disclose expressly or inherently, using the composition to treat sunburn).

In this case, the Examiner acknowledges that Migliaccio et al. does not expressly disclose increasing resistance to oxidative stress or the benefits of disruption p66shc signaling. If such modulation were accidentally or unwittingly achieved while Migliaccio et al. were in pursuit of something different, it would be illogical to say this constitutes an anticipation. Notably, this result is consistent with the reasoning of the U.S. Supreme Court which stated in *Tilghman v. Proctor*, 102 U.S. 707 (1881), that if a compound was "accidentally and unwittingly produced, whilst the operators where in pursuit of other and different results, without exciting attention and without it being known what was done or how it had been done, it would be absurd to say that this was an anticipation." Here, Migliaccio et al. provides no indication that the plasmids employed were capable of modulating resistance to oxidative stress in the cells studied.

Given that inherent anticipation requires certainty, cases have held that a prior accidental achievement of a product or process does not constitute inherent anticipation since a true accidental achievement provides the public no assurance that others can achieve the same result at a later time. 1 Chisum on Patents, §3.03; *In re Seaborg*, 328 F.2d 996 (C.C.P.A. 1964); *Eibel Process Co. v. Minnesota & Ontario Paper Co.*, 261 US 45 (1923).

Before the Federal Circuit decision in *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373 (Fed. Cir 2003), inherency cases fit into two different categories. One line of cases suggested that inherency required recognition of the inherent characteristic or effect by one of skill in the art. See e.g.

Continental Can, 948 F.2d at 1268; *Glaxo Inc. v. Novopharm Ltd*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). The second line suggested that recognition of the inherent feature by a skilled artisan is not required. See e.g. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999); *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1345 (Fed. Cir. 2002). This inconsistency prompted the clarification between different types of claims in *EMI Group of North America, Inc. v. Cypress Semiconductor Corp.*, 268 F.3d 1342 (Fed. Cir. 2001). *EMI* noted that recognition by a skilled artisan "may be sensible" when the recited matter is a structure or a method step. Id. at 1350-1351.

In *Schering*, the Court distinguished the facts from previous cases where the prior art did not definitively demonstrate the claimed subject matter. The *Schering* decision expressly rejected the "recognition" element, and allowed the Federal Circuit to undercut the doctrine of accidental anticipation by focusing exclusively on the "necessity" requirement of inherent anticipation. 339 F.3d at 1378. The analysis provided in the *Schering* petition for rehearing *en banc* demonstrates that all the judges on the Federal Circuit do not share the same interpretation of the "recognition" requirement that the three judge panel followed in deciding the case. 348 F.3d 992, 993-996 (Fed Cir. 2003) (Judges Lourie and Newman dissenting). The three judge panel opinion certainly cannot trump the Supreme Court (i.e., *Tilghman*). Moreover, the PTO is bound by prior decisions of the Federal Circuit and its predecessor courts, unless they are overruled by the Federal Circuit sitting *en banc*. *Ex parte Nesbit*, 25 U.S.P.Q. 1817 (P.T.O. B.P.A.I. 1992). However, as mentioned above, quite apart from the "recognition" requirement, the "necessity" requirement has not been satisfied by Migliaccio et al.

The granting of a patent on claim 9 is justified because

Applicants discovered that nucleic acids which hybridize to SEQ ID NO: 2 are capable of modulating resistance to oxidative stress and/or disrupting the $p66^{shc}$ signaling pathway, and the public gains knowledge of the process in return for the temporary exclusive right of a patent. Applicants do not seek to exclude the public from practicing the prior art as taught by Migliaccio et al. For the above reasons, Applicants respectfully request withdrawal of the §102(b) rejection of claim 9.

CLAIMS 9-10, 22-25, 27, 36-37, AND 46-52, AS AMENDED SATISFY THE WRITTEN DESCRIPTION REQUIREMENT OF 35 USC §112, FIRST PARAGRAPH

The Examiner has rejected claim 9-10, 12, 19-25, 27, 36-37, 46-52 under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement.

Specifically, the Examiner asserts that the claims encompass a genus of $p66^{SHC}$ molecules which are not adequately described and do not set forth a particular sequence for $p66^{SHC}$ molecules encompassed by the claims. Furthermore, the Examiner states that the specification does not adequately describe the genus of agents that are capable of modulating $p66^{SHC}$ expression. Applicants respectfully disagree.

As noted in the M.P.E.P. at §2163, "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention."

Notably, both the nucleic acid and amino acid sequences of $p66^{SHC}$ are provided in the specification in Figure 5, which has been amended in this response to add sequence identifiers. The amended claims now set forth a sequence for $p66^{SHC}$ molecules (e.g. nucleic acids which specifically hybridize to SEQ ID NO: 2) and clearly define the agents that modulate

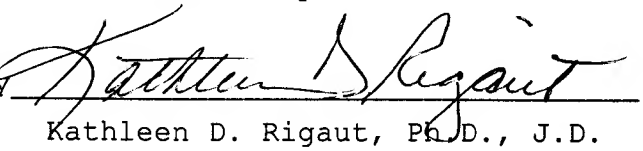
resistance to oxidative stress. In fact, at page 8, the Examiner states that "[t]he only member of the genus which appears to be adequately described is the amino acid sequence that is SEQ ID NO: 2 and the nucleotide sequences which would encode SEQ ID NO: 2 (which includes the sequence that is SEQ ID NO: 1)." Also, at page 9 the Examiner states that "the specification has described … an antisense nucleic acid sequence which specifically hybridizes to a nucleotide sequence which encodes the $p66^{SHC}$ protein that is SEQ ID NO: 2 [and] is an inhibitor of $p66^{SHC}$ expression." Applicants have amended the claims to recite the specific sequence identifiers, and have indicated that the agent is a nucleic acid, more specifically in certain dependent claims, an antisense oligonucleotide. Applicants submit that amended claims provide sufficient identifying characteristics of the invention to meet the written description requirement under 35 U.S.C. §112, first paragraph. Accordingly, Applicant request that the rejection of the claims on this basis be withdrawn.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the January 8, 2008, Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to call the undersigned agent at the phone number given below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By 

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Enclosures: (1) Notice to Comply